

The Center for Microarray Technology

1st year applicant

Steve Blair and Alex Chagovetz
Electrical and Computer Engineering
University of Utah

Center Mission

The Center for Microarray Technology (CMT) will develop highly parallel microarray technologies with applications in genomics, pharmaco-genomics, molecular diagnostics, and proteomics.

“At the University of Utah in Salt Lake City, Steve Blair is taking a different approach.... The beauty of this approach is that virtually eliminates unwanted fluorescence from unbound species.... [It combines] research in the physical sciences with research in the life sciences, and ... could have applications throughout the worlds of biology and medicine.”

- Brenda Korte, Health Scientist Administrator
NIH's National Institute of Biomedical Imaging and
Bioengineering (NIBIB), Optics & Photonics News, 2003

Core Technologies

Metallic nanocavity arrays

- Inexpensive and disposable microarray substrate used in standard hybridization chambers and array scanners.
- >12x improvement in sensitivity (>30x predicted)
- > 7x increase in fluorescence yield (>10x predicted)

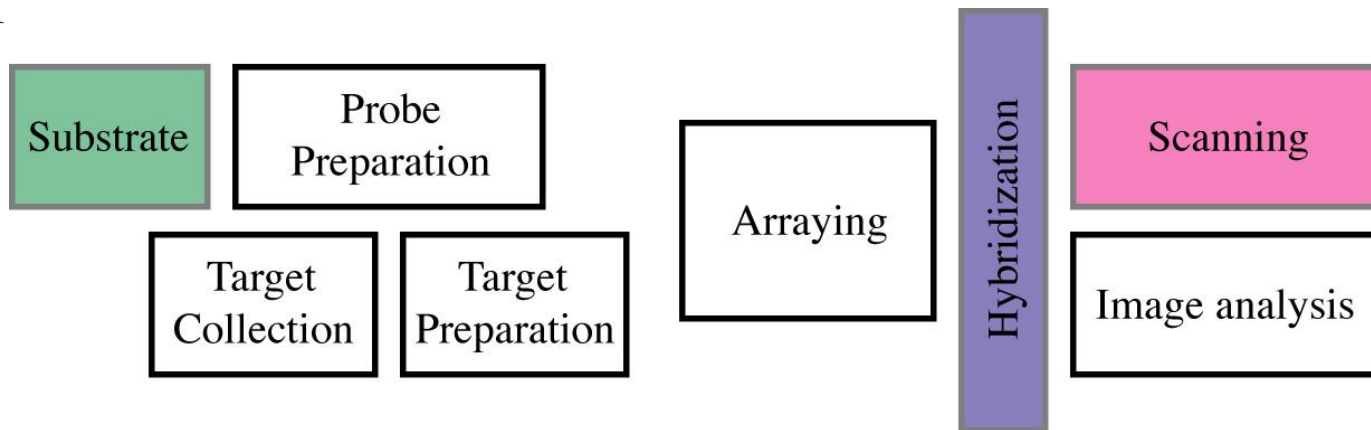
Sequential microfluidics

- Sample delivery to improve microarray hybridization efficiency.
- 100x reduction in hybridization times
- Modified hybridization kinetics

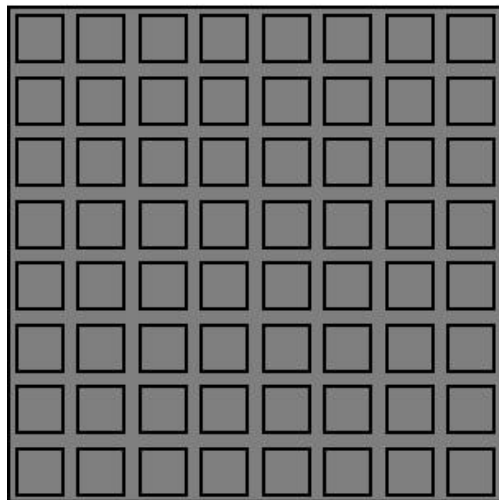
Real-time detection and analysis

- Significantly improves the quality of data over current platforms.
- Increased dynamic range ($\sim 10^5$)
- Improved data quality (i.e. target specificity)
- Reduced assay time

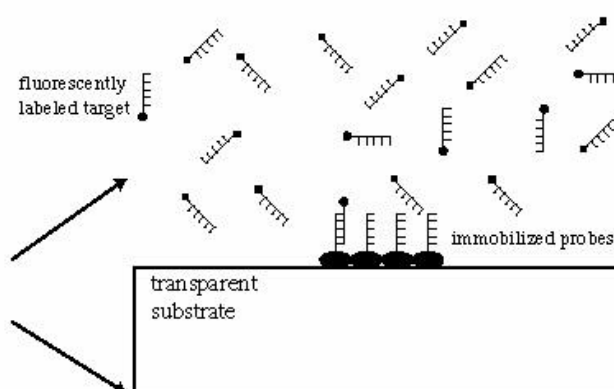
Current Microarray Technology



Hybridization array

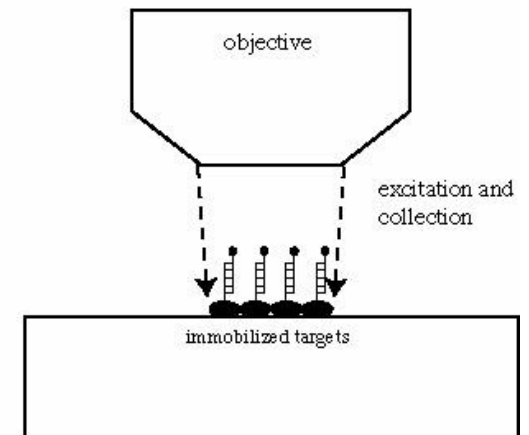


Individual hybridization zone



- 12-48 hour hybridization time
- 10,000 or more spots
- sub-nM target concentrations

Read-out at endpoint



- read with scanner or imager
- complex referencing schemes

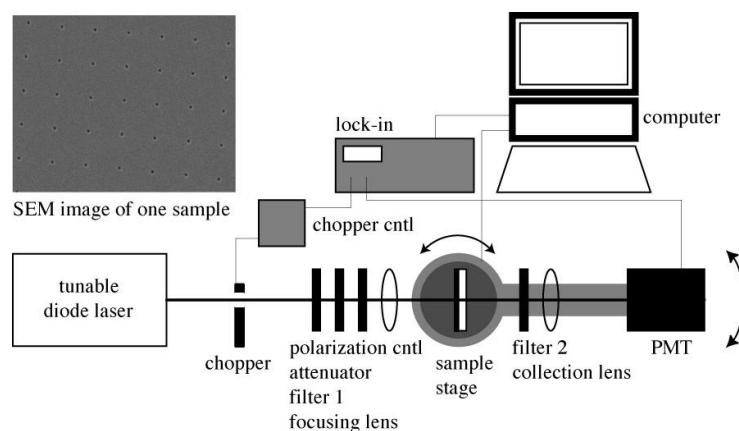
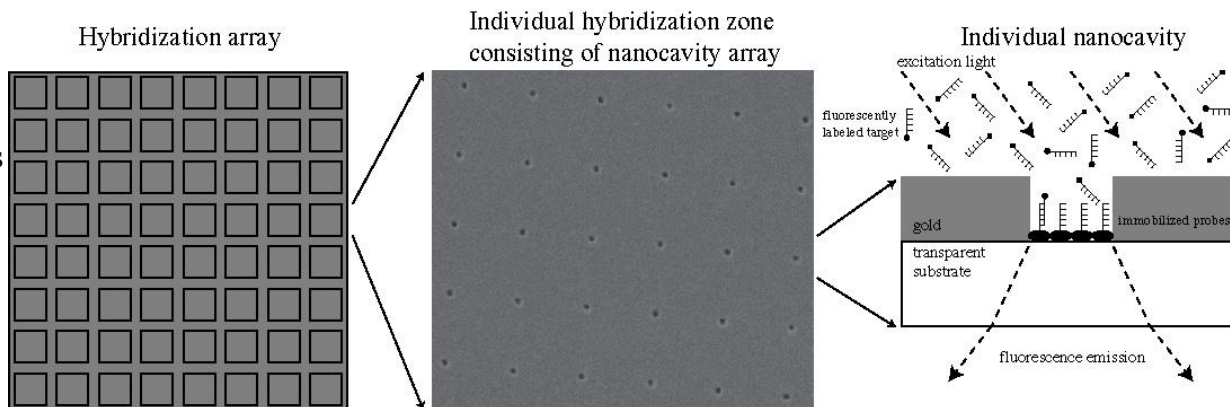
Metallic Nanocavity Substrates

Concept

- nanocavities serve as detection sites
- probe molecules bound in nanocavities
- target molecules bind to probes

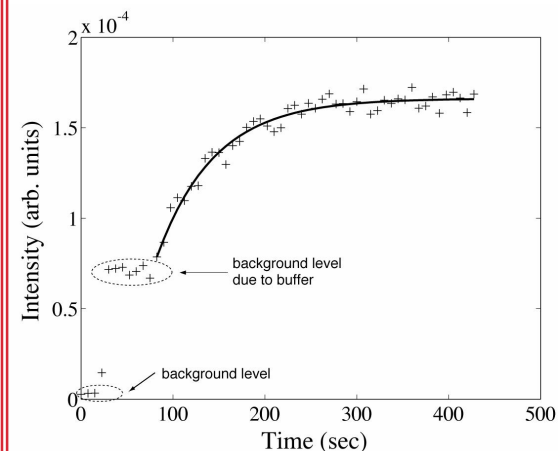
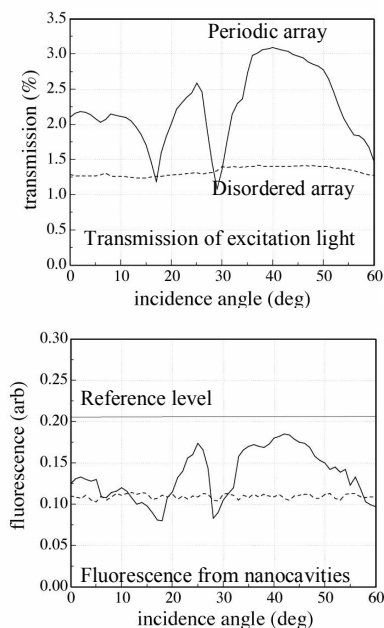
Advantages

- increased fluorescence yield
- increased excitation intensity
- increased background isolation
- improved sensitivity



Experimental results

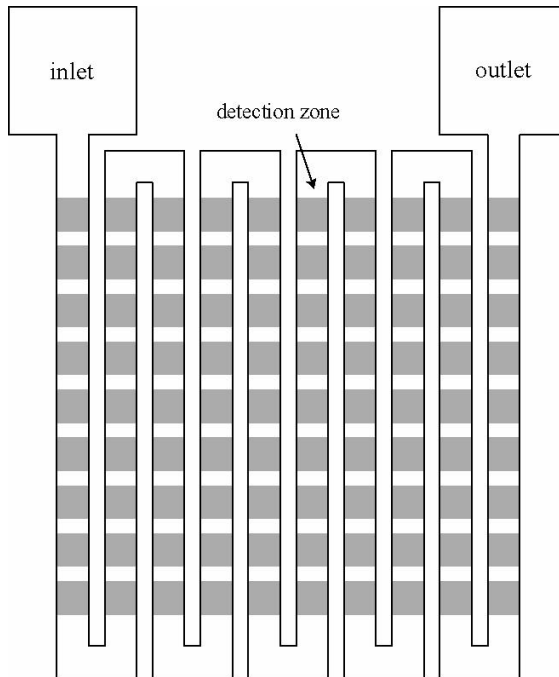
- transmission peaks due to surface plasmon excitation
- fluorescence peaks under same conditions
 - >2x excitation enhancement
 - 7x yield enhancement
 - verified by simulations



Real-time DNA detection

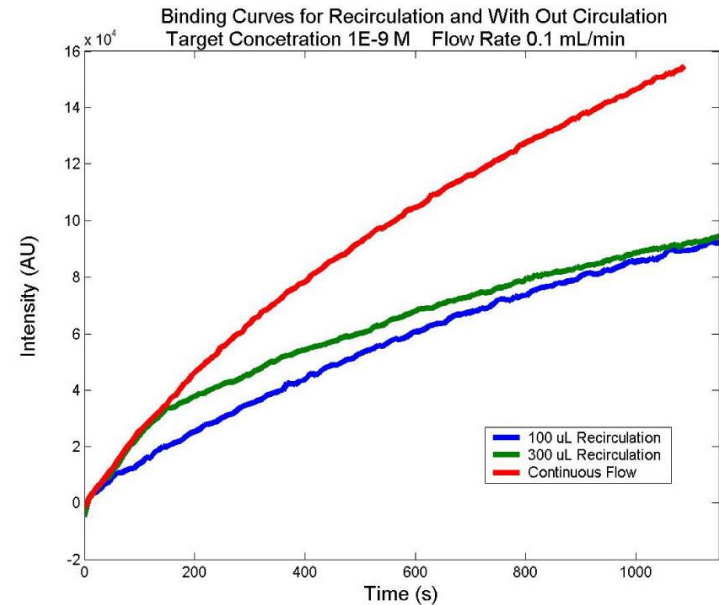
- anti-T3 probe oligo bound in nanocavities
- T3 target oligos introduced in solution
- hybridization kinetics measured
- >100x increase in signal to background

Sequential Microfluidics



Microfluidic sequential delivery

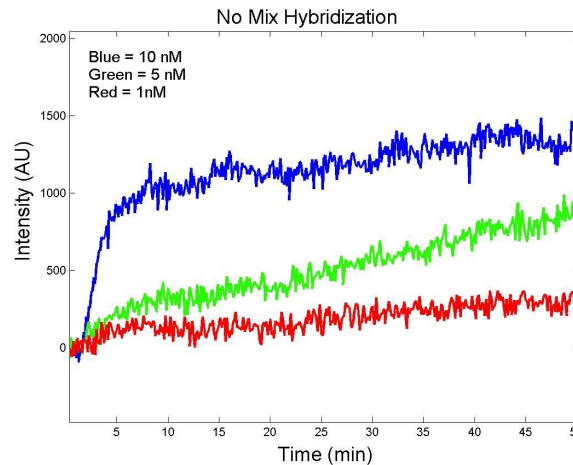
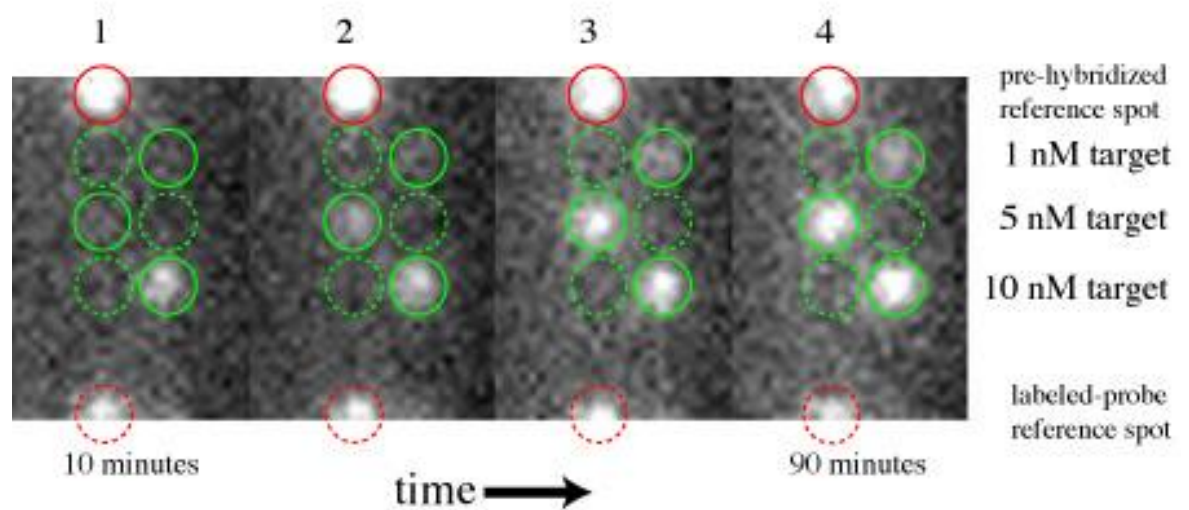
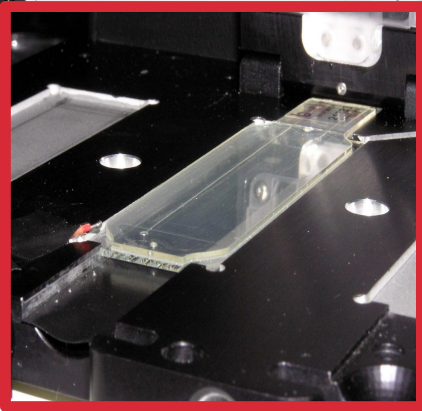
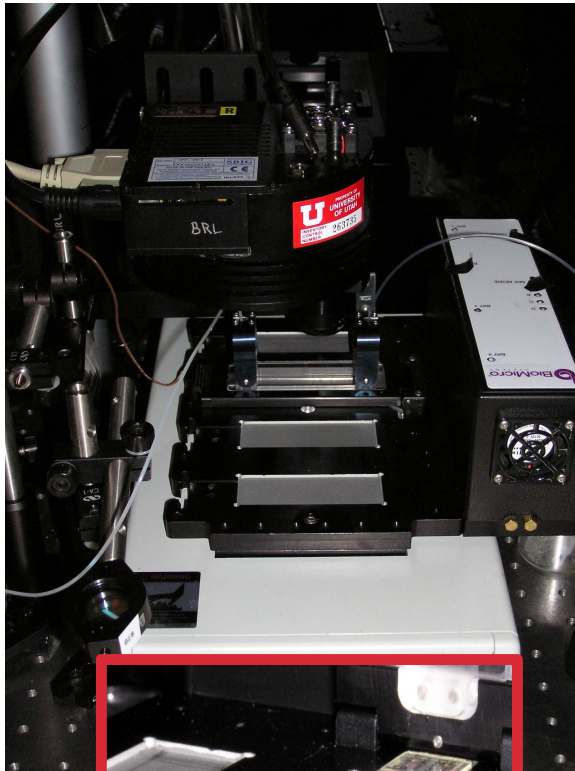
- eliminate lateral diffusion
- maintain reaction-limited kinetics
- flow-through system for large sample volumes



Sample recirculation

- minimize sample volume
- maximize binding efficiency

Real-Time Platform



- Can ultimately image
> 10,000 zones in real-time
- Kinetics can be used to:
 - detect non-specific binding
 - detect hetero-duplex formation
 - improve data quality
 - increase dynamic range

Microarray Technology IP

Patents

Optical microcavities for high-throughput biosensing	Patented Licensed
Microfluidic platforms for use with specific binding assays, specific binding assays that employ microfluidics, and methods	Pending
Biosensors including metallic nanocavities	Provisional

Technology Disclosures

Additional technologies related to nanocavities, microfluidics, and real-time analysis:

Methods to Improve Hybridization Selectivity on a Microarray	Disclosure
Electrophoretic Delivery of DNA to Nanostructures	Disclosure
Metallic Nanostructure-Enhanced FRET	Disclosure
Method for Surface-Selective Fluorescence Detection	Disclosure

Microarray Substrate Market

Market Size

- 2004 - \$152M (approx. 15M substrates)
- 2010 - \$282M (approx. 28M substrates)
- Growth of 11% per year

Market Details

- Concentrated on new surface chemistries
- Few developing substrate technologies
- ➡ few competitors, many customers

“The Enhanced Microarray Substrate being developed by Center for Microarray Technology will be uniquely positioned since it is not tied to any particular printing or spotting technology – it will enhance performance of all alternatives.” Lloyd Alexander, COEP consulting report.

Commercialization Plan

Nanocavity array substrate

- Spin-off company
- Invest in low-cost volume manufacturing
 - outsource standard microlithography
 - micromolding technologies (i.e. CD's, DVD's)
- Identify distribution partners
 - existing distributors (Fisher, PerkinElmer, TelChem)
 - platform makers (Agilent, BioMicro)
 - generate cash flow for further development (real-time platform)

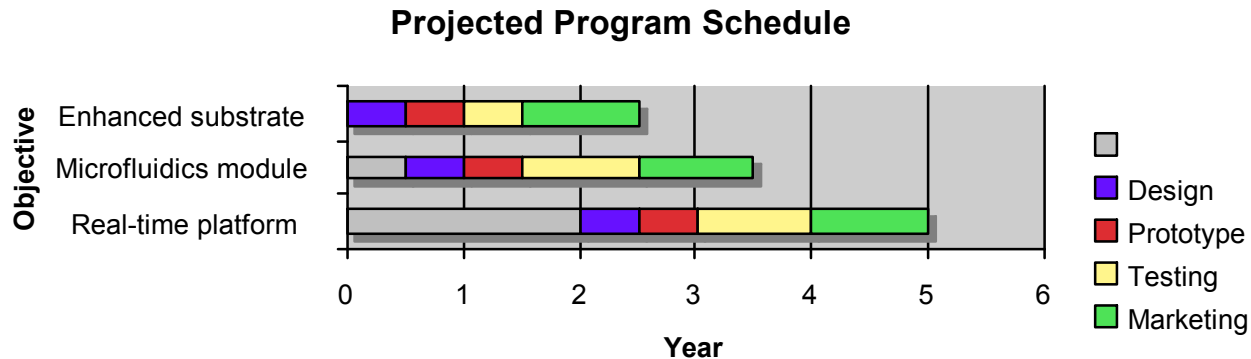
Microfluidics module

- Identify unique applications (e.g. pathogen screening)
- Identify development partner (with existing platform)
- License technology

Real-time platform

- Pursue grants/contracts for specialty applications
- Define potential markets, develop prototypes

Timeline



Nanocavity array substrate

Year 1

- geometry optimization
- surface chemistry/testing
- prototype development
- market analysis

Year 2

- applications/field testing
- production ramp-up
- identify marketing/distribution partners

CMT Funding

(expired)	Whitaker Foundation	Optical microcavities for high-throughput biosensors	1/1/00-4/30/03	\$210,000
(expired)	NIH R-21	Exploration of metallic nanoparticle biosensors	4/1/02-3/31/04	\$206,876
(current)	NSF	Integrated-optic nanoparticle biosensor arrays	2/15/02-2/28/07	\$375,000
(pending)	COEP	Center for Microarray Technology	7/1/05-6/30/06 7/1/06-6/30/07	\$150,000 \$150,000
(pending)	NIH R-21	A real-time nucleic acid array platform with enhanced specificity	12/1/05-11/30/07	\$393,800
(pending)	NIH R-01	Quantitative study of fluorescence transduction by periodic metallic nanostructures	12/1/05-11/30/09	\$1,241,050
(pending)	NIH R-01	Biosensing based upon molecular confinement in an array of metallic nanocavities	5/1/06-4/30/10	\$1,300,000

Principals

Steve Blair, PhD (Electrical Engineering)

Expertise

Optical techniques in molecular detection

Fabrication of nanoscale and microscale optical, mechanical, fluidic, and thermal structures

Integration of these technologies into working systems and performance analysis

Prof. Blair has presented his optical biosensor research at numerous international conferences
27 journal publications and over 40 conference publications

Served and continues to serve as a consultant in the biomedical instrumentation industry.

Alex Chagovetz, PhD (Biophysics)

Expertise

Dr. Chagovetz has strong international and local industry experience and contacts

Specific expertise in fluorescence-based assay methods, PCR, and microarray analysis techniques

Previous experience

Assistant Professor in the Kiev School of Medicine

Research Fellow at the Eccles Institute of Human Genetics

Senior Scientist at Idaho Technology

Collaborated with Alpha Helix AB, Uppsala Sweden; Fluorescent Genomics, Inc.; and Epoch Biosciences, Inc.

Advisory Group

Lloyd Alexander, MBA

COEP Consultant, Elbow Fork Partners

Kurt Dobson

Successful entrepreneur in high technology

Karl Voelkerding, MD

Medical Director, Molecular Diagnostics, ARUP

Nils Adey, PhD

Chief Scientist, BioMicro Systems